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=> fil reg
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STRUCTURE FILE UPDATES:   11 MAY 2005  HIGHEST RN 850303-40-1
DICTIONARY FILE UPDATES:  11 MAY 2005  HIGHEST RN 850303-40-1

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*                                                                       *
* The CA roles and document type information have been removed from     *
* the IDE default display format and the ED field has been added,       *
* effective March 20, 2005.  A new display format, IDERL, is now        *
* available and contains the CA role and document type information.     *
*                                                                       *
*************************************************************************

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Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide can tot l6

L6   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   384832-65-9  REGISTRY
ED   Entered STN:  20 Jan 2002
CN   2H-Indol-2-one, 3-[(3-fluoro-4-methoxyphenyl)methylene]-1,3-dihydro- (9CI)
     (CA INDEX NAME)
MF   C16 H12 F N O2
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL
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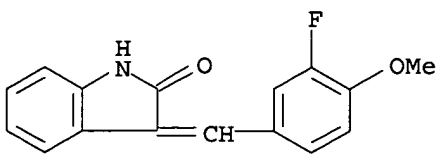


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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              3 REFERENCES IN FILE CA (1907 TO DATE)
              3 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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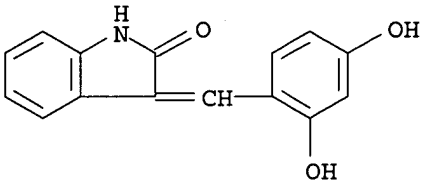
REFERENCE 1: 139:207829

REFERENCE 2: 138:131086

REFERENCE 3: 136:64633

L6 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **328106-29-2** REGISTRY
ED Entered STN: 20 Mar 2001
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN MAE 87
MF C15 H11 N O3
SR Chemical Library
LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER, USPATFULL



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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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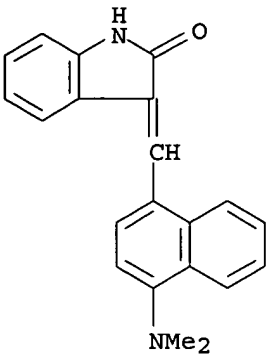
REFERENCE 2: 139:207829

REFERENCE 3: 138:131086

REFERENCE 4: 136:64633

L6 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **163655-37-6** REGISTRY
ED Entered STN: 08 Jun 1995
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C21 H18 N2 O
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, PROUSDDR, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:207829

REFERENCE 2: 138:131086

REFERENCE 3: 136:64633

REFERENCE 4: 122:316911

=> fil uspatall
FILE 'USPATFULL' ENTERED AT 12:20:15 ON 12 MAY 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

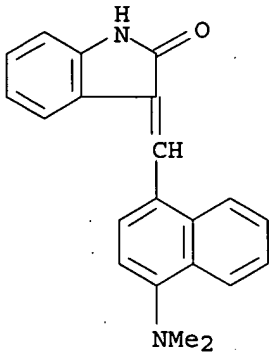
FILE 'USPAT2' ENTERED AT 12:20:15 ON 12 MAY 2005
CA INDEXING COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr tot l9

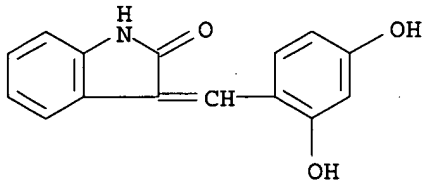
L9 ANSWER 1 OF 3 USPATFULL on STN
AN 2004:315288 USPATFULL
TI Kinase inhibitors and the use thereof
IN Chirchin, Vladimir, Frankkfurt am Main, GERMANY, FEDERAL REPUBLIC OF
Athanassios, Giannis, Leipzig, GERMANY, FEDERAL REPUBLIC OF
Mazitschek, Ralph, Boston, MA, UNITED STATES
Sleemann, Jonathan, Bruchsal, GERMANY, FEDERAL REPUBLIC OF
PI US 2004248965 A1 20041209
AI US 2004-483687 A1 20040706 (10)
WO 2002-EP7778 20020712
PRAI DE 2001-134196 20010713
DT Utility
FS APPLICATION
LREP Friedrich Kueffner, Suite 910, 317 Madison Avenue, New York, NY, 10017
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to protein kinase inhibitors and to the

use thereof for the treatment of diseases induced by pathological signal transduction cascades.

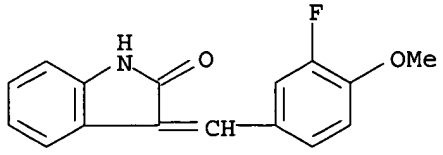
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **163655-37-6P 328106-29-2P 384832-65-9P**
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)
RN 163655-37-6 USPATFULL
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 328106-29-2 USPATFULL
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



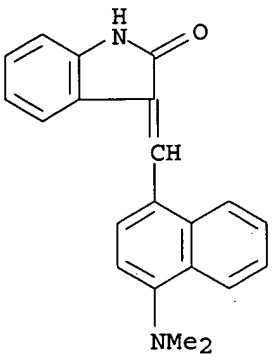
RN 384832-65-9 USPATFULL
CN 2H-Indol-2-one, 3-[(3-fluoro-4-methoxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



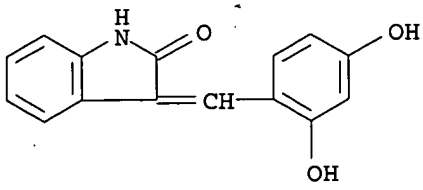
L9 ANSWER 2 OF 3 USPATFULL on STN
AN 2003:257244 USPATFULL
TI Methods of extending corneal graft survival
IN DeVries, Gerald W., Laguna Hills, CA, UNITED STATES
PI US 2003180294 A1 20030925

AI US 2002-81126 A1 20020222 (10)
DT Utility
FS APPLICATION
LREP CATHRYN CAMPBELL, CAMPBELL & FLORES LLP, 7th Floor, 4370 La Jolla Village Drive, San Diego, CA, 92122
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 2079
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of extending corneal graft survival following corneal transplantation in a patient by administering to the patient an effective amount of a pharmaceutical composition containing a vascular endothelial growth factor receptor-3 (VEGFR-3) inhibitor, whereby lymphangiogenesis is suppressed in the cornea of the patient.

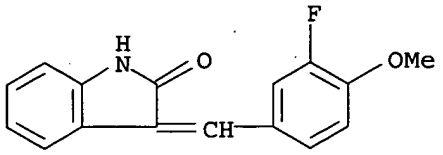
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **163655-37-6P 328106-29-2P 384832-65-9P**
(preparation of indolin-2-ones as VEGFR-3 inhibitors to increase corneal graft survival)
RN 163655-37-6 USPATFULL
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 328106-29-2 USPATFULL
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 384832-65-9 USPATFULL
CN 2H-Indol-2-one, 3-[(3-fluoro-4-methoxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



L9 ANSWER 3 OF 3 USPATFULL on STN
AN 97:37980 USPATFULL
TI Bulk dyeing of plastics
IN Roschger, Peter, Koln, Germany, Federal Republic of
PA Bayer Aktiengesellschaft, Leverkusen, Germany, Federal Republic of (non-U.S. corporation)
PI US 5626633 19970506
AI US 1995-566317 19951201 (8)
RLI Continuation of Ser. No. US 1994-263222, filed on 21 Jun 1994, now abandoned
PRAI DE 1993-4321420 19930628
DE 1993-4340560 19931129
DT Utility
FS Granted
EXNAM Primary Examiner: Lieberman, Paul; Assistant Examiner: Dusheck, Caroline L.
LREP Sprung Horn Kramer & Woods
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 969
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Dyestuffs of the formula (I) ##STR1## wherein n denotes 1 or 2,

T denotes O or N--R.sub.0, wherein

R.sub.0 denotes H, alkyl, aryl or acyl or, together with R.sub.2 or R.sub.3, forms a 5- to 7-membered ring,

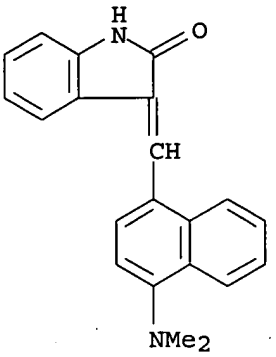
R.sub.1 if n=1, denotes aryl, hetaryl or heterocyclylidenemethyl and

if n=2, denotes a direct bond or arylene and

R.sub.2 and R.sub.3 are independent or cyclic radicals having the meanings given in the description,

are employed for bulk dyeing of plastics, preferably thermoplastics.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **163655-37-6P**
(dyes for bulk dyeing of plastics)
RN 163655-37-6 USPATFULL
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:20:28 ON 12 MAY 2005

FILE COVERS 1907 - 12 May 2005 VOL 142 ISS 20
FILE LAST UPDATED: 11 May 2005 (20050511/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> => d l14 all hitstr tot

L14 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:717219 HCAPLUS
DN 141:388594
ED Entered STN: 02 Sep 2004
TI Local injection of receptor tyrosine kinase inhibitor **MAE 87** reduces retinal neovascularization in mice
AU Unsoeld, Anke S.; Junker, Bernd; Mazitschek, Ralph; Martin, Gottfried; Hansen, Lutz L.; Giannis, Athanassios; Agostini, Hansjuergen T.
CS Department of Ophthalmology, University of Freiburg, Freiburg, Germany
SO Molecular Vision (2004), 10, 468-475
CODEN: MVEPFB; ISSN: 1090-0535
URL: http://www.molvis.org/molvis/v10/a60/unsoeld.pdf
PB Molecular Vision
DT Journal; (online computer file)
LA English

CC 1-12 (Pharmacology)

AB Purpose: Retinal neovascularization occurs under the influence of angiogenic factors like vascular endothelial growth factor (VEGF). VEGF signaling is enhanced by insulin-like growth factor-1 (IGF-1). In vitro, the oxoindolinone **MAE 87** inhibits angiogenic signal transduction by blocking tyrosine kinase receptors including VEGF receptor 2 (VEGFR-2), IGF-1R, fibroblast GF-1R and epidermal GFR. We investigated the effect of **MAE 87** in vivo using the mouse model for oxygen induced retinopathy. Methods: From postnatal day seven (P7) on, C57BL/6J mice were kept in a 75% oxygen environment for five days. On postnatal day 12 (P12) they received an intravitreal injection of **MAE 87** in one eye and control substance in the fellow eye. The animals were sacrificed by intracardial perfusion with fluorescein-dextran solution on P17. Retinal whole mounts were prepared and ischemic retinopathy was evaluated in 26 animals using a standardized retinopathy score. Results: After a single intravitreal injection of **MAE 87** there were significantly less angioproliferative changes (blood vessel tufts, extra-retinal neovascularization, and blood vessel tortuosity) than in the fellow eye ($p=0.007$). The median retinopathy score (maximal 13) for the **MAE 87** treated eyes was 6 (25th percentile: 5; 75th percentile: 7) and 8 for the control eyes (25th percentile: 5; 75th percentile: 10). Conclusions: The tyrosine kinase inhibitor **MAE 87** may be a promising substance for local treatment of retinal neovascularization. Due to its ability to inhibit not only the VEGF but also the IGF-1 cascade, **MAE 87** may prove especially valuable for the treatment of diabetic retinopathy.

ST **MAE87** proliferation inhibition retina neovascularization mouse

IT Cell proliferation
(inhibition; single intravitreal injection of **MAE 87** significantly reduced angioproliferative changes in mouse model of oxygen induced retinopathy)

IT Angiogenesis
(neovascularization, retinal; single intravitreal injection of **MAE 87** significantly reduced angioproliferative changes in mouse model of oxygen induced retinopathy)

IT Angiogenesis
(neovascularization; single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

IT Eye, disease
(retina, neovascularization; single intravitreal injection of **MAE 87** significantly reduced angioproliferative changes in mouse model of oxygen induced retinopathy)

IT Eye
(retina; single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

IT Eye, disease
(retinopathy; single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

IT 67763-96-6, Insulin-like growth factor-1 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal

neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

IT **328106-29-2, MAE 87** 340830-03-7, Receptor tyrosine kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

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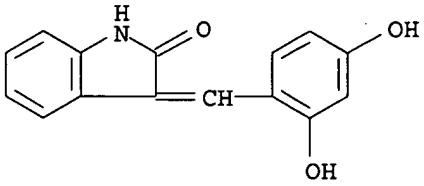
IT **328106-29-2, MAE 87**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single intravitreal injection of RTK inhibitor **MAE 87** significantly reduced oxygen induced retinal neovascularization possibly by inhibiting VEGF, IGF-1 cascade in mouse model of oxygen induced retinopathy)

RN 328106-29-2 HCAPLUS
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



L14 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:696673 HCAPLUS
DN 139:207829
ED Entered STN: 05 Sep 2003
TI Methods of extending corneal graft survival using VEGFR-3 inhibitors which inhibit lymphangiogenesis
IN **De Vries, Gerald W.**
PA **Allergan, Inc., USA**
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-12 (Pharmacology)
Section cross-reference(s): 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003072029	A2	20030904	WO 2003-US5125	20030220 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003180294	A1	20030925	US 2002-81126	20020222 <--
	CA 2476994	AA	20030904	CA 2003-2476994	20030220 <--
	EP 1476187	A2	20041117	EP 2003-711158	20030220 <--
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PRAI	US 2002-81126	A	20020222 <--		
	WO 2003-US5125	W	20030220 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

WO 2003072029	ICM	A61K
US 2003180294	NCL	424/143.100; 514/044.000
	ECLA	A61K031/00; A61K031/404; A61K031/404+M; A61K045/06 <--

AB The present invention provides a method of extending corneal graft survival following corneal transplantation in a patient by administering to the patient an effective amount of a pharmaceutical composition containing a vascular endothelial growth factor receptor-3 (VEGFR-3) inhibitor, whereby lymphangiogenesis is suppressed in the cornea of the patient. More specifically, the VEGFR-3 inhibitor is a dominant neg. VEGFR-3 receptor, a nucleic acid encoding a dominant neg. VEGFR-3 receptor, a VEGFR-3 kinase inhibitor, an ATP analog, a VEGFR-3 binding mol., or a sequence-specific RNase.

ST corneal graft survival VEGFR3 inhibitor lymphangiogenesis suppression

IT Protein motifs
(VEGFR-3 extracellular domain as inhibitor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Enzyme functional sites
(active, inhibitor binds to the VEGFR-3 catalytic domain; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Angiogenesis inhibitors
Immunosuppressants
(addnl. therapeutic agent; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-VEGFR-3; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Antisense nucleic acids
Ribozymes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as inhibitor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Eye
(cornea, transplant; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Transplant and Transplantation
(cornea; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Nucleic acids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encoding VEGFR-3 dominant neg. receptor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Lymphatic system
(lymph vessel, lymphangiogenesis; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Angiogenesis
(lymphangiogenesis; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Human
(methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal, anti-VEGFR-3; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Vascular endothelial growth factor receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type VEGFR-3, dominant neg. VEGFR-3 receptor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VEGFR-3; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT 144638-77-7, VEGFR-3 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT 56-65-5D, 5'-ATP, analogs, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

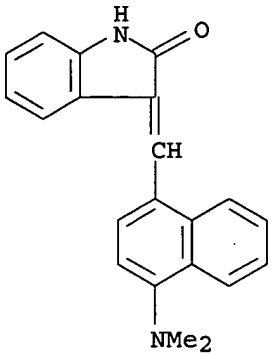
IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolin-2-ones as VEGFR-3 inhibitors to increase corneal graft survival)

IT 59-48-3, Indolin-2-one 95-01-2, 2,4-Dihydroxy benzaldehyde 351-54-2, 3-Fluoro-4-methoxybenzaldehyde 1971-81-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of indolin-2-ones as VEGFR-3 inhibitors to increase corneal graft survival)

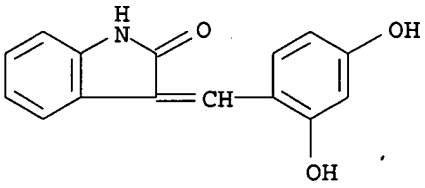
IT 9001-99-4, Ribonuclease
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequence specific RNase as inhibitor; methods of extending corneal graft survival using VEGFR-3 inhibitors to inhibit lymphangiogenesis)

IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indolin-2-ones as VEGFR-3 inhibitors to increase corneal graft survival)

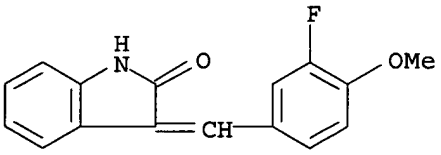
RN 163655-37-6 HCAPLUS
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 328106-29-2 HCAPLUS
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 384832-65-9 HCAPLUS
CN 2H-Indol-2-one, 3-[(3-fluoro-4-methoxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



L14 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:76607 HCAPLUS
DN 138:131086
ED Entered STN: 31 Jan 2003
TI Indolin-2-one derivative protein kinase inhibitors, their preparation, and their therapeutic use
IN Chirchin, Vladimir; Athanassios, Giannis; Mazitschek, Ralph; Sleeman, Jonathan
PA Forschungszentrum Karlsruhe Gmbh, Germany
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K031-404
ICS C07D209-34; A61P035-00
CC 1-6 (Pharmacology)

Section cross-reference(s): 27

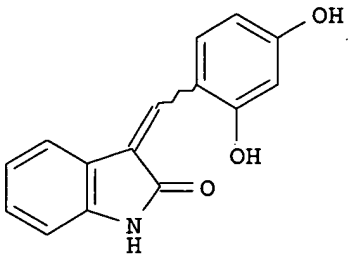
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003007943	A1	20030130	WO 2002-EP7778	20020712
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10134196	A1	20030424	DE 2001-10134196	20010713
	DE 20122287	U1	20050421	DE 2001-20122287	20010713
	EP 1406615	A1	20040414	EP 2002-762351	20020712
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2004536127	T2	20041202	JP 2003-513551	20020712
	US 2004248965	A1	20041209	US 2004-483687	20040706
PRAI	DE 2001-10134196	A	20010713		
	WO 2002-EP7778	W	20020712		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003007943	ICM	A61K031-404
	ICS	C07D209-34; A61P035-00
WO 2003007943	ECLA	C07D209/34
DE 10134196	ECLA	A61K031/404; C07D209/34
JP 2004536127	FTERM	4C086/AA01; 4C086/AA02; 4C086/BC13; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA36; 4C086/ZB21; 4C086/ZB26; 4C086/ZB39; 4C086/ZC20; 4C086/ZC42; 4C204/BB01; 4C204/CB03; 4C204/DB13; 4C204/DB15; 4C204/DB30; 4C204/EB03; 4C204/FB01; 4C204/GB01
US 2004248965	NCL	514/418.000; 548/484.000
	ECLA	A61K031/404; C07D209/34

GI



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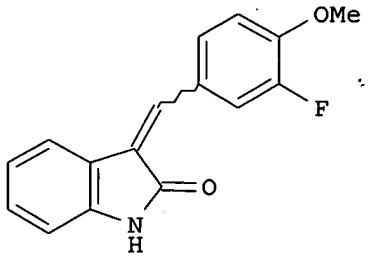
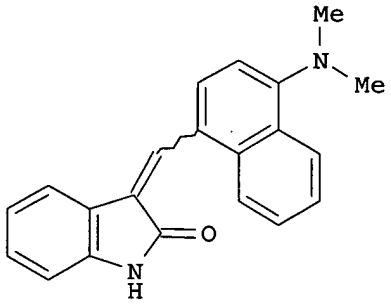


II



III

AB The invention discloses protein kinase inhibitors I, II, and III (preparation of these compds. is described) and the use thereof for treating diseases that are triggered by pathol. signal transduction cascades, e.g. cancer.

ST indolinone deriv prepn protein kinase inhibitor therapeutic; antitumor indolinone deriv protein kinase inhibitor; signal transduction disease therapeutic indolinone deriv protein kinase inhibitor

IT Animal cell line
(1AS; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Animal cell line
(HUVEC, endothelial cell proliferation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Angiogenesis
(and lymphangiogenesis; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Phosphorylation, biological
(autophosphorylation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Mammary gland, neoplasm
(carcinoma; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Blood vessel
(endothelium, endothelial cell proliferation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Infection
(filariasis; indolinone derivative protein kinase inhibitor preparation and therapeutic use)

IT Angiogenesis inhibitors
Antitumor agents
Apoptosis
Cell proliferation
Cytotoxic agents

Human
Neoplasm
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT Carcinoma
(mammary; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT Endothelium
(microvascular, HDMEC cells, endothelial cell proliferation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT Blood vessel
(microvessel, endothelium, HDMEC cells, endothelial cell proliferation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT Phosphorylation, biological
(protein; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT Endothelium
(vascular, endothelial cell proliferation; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT 59-48-3D, Indolin-2-one, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT 59-48-3 95-01-2, 2,4-Dihydroxybenzaldehyde 351-54-2, 3-Fluoro-4-methoxybenzaldehyde 1971-81-9, 4-Dimethylamino-1-naphthaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)
IT 79079-06-4, EGFR tyrosine kinase 103843-29-4, IGF1-R kinase 137632-09-8, ErbB2 receptor tyrosine kinase 144638-77-7, VEGFR-3 kinase 148047-29-4, TIE2 receptor kinase 150027-15-9, Gene FGFR1 tyrosine kinase 150977-45-0, VEGFR2 kinase 340830-03-7, Receptor tyrosine kinase 372092-80-3, Protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; indolinone derivative protein kinase inhibitor preparation and therapeutic use)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WAHL; BAGARD: BULL SOC CHIM FR 1909, V4(5), P1038
(2) Bayer Ag; EP 0632102 A 1995 HCAPLUS
(3) Blum; BIOCHEMISTRY 2000, V39(51), P15705 HCAPLUS
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(5) Kirkin, V; EUR J BIOCHEM 2001, V268, P5530 HCAPLUS
(6) McNutt, R; WO 9910325 A 1999 HCAPLUS
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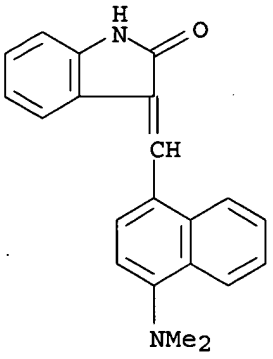
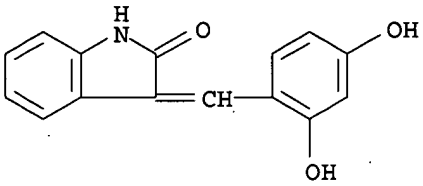
(8) Sugen Inc; WO 9640116 A 1996 HCAPLUS
IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indolinone derivative protein kinase inhibitor preparation and therapeutic use)

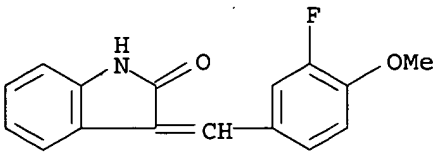
RN 163655-37-6 HCAPLUS
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 328106-29-2 HCAPLUS
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 384832-65-9 HCAPLUS
CN 2H-Indol-2-one, 3-[(3-fluoro-4-methoxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



L14 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:811951 HCAPLUS
DN 136:64633
ED Entered STN: 08 Nov 2001
TI Characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2
AU Kirkin, Vladimir; Mazitschek, Ralph; Krishnan, Jaya; Steffen, Anja; Waltenberger, Johannes; Pepper, Michael S.; Giannis, Athanassios; Sleeman, Jonathan P.
CS Forschungszentrum Karlsruhe, Institute of Genetics, Karlsruhe, D-76021, Germany
SO European Journal of Biochemistry (2001), 268(21), 5530-5540

jan delaval - 12 may 2005

CODEN: EJBCAI; ISSN: 0014-2956
PB Blackwell Science Ltd.
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3
AB VEGF-C and VEGF-D are lymphangiogenic factors that bind to and activate VEGFR-3, a fms-like tyrosine kinase receptor whose expression is limited almost exclusively to lymphatic endothelium in the adult. Processed forms of VEGF-C and VEGF-D can also activate VEGFR-2, a key player in the regulation of angiogenesis. There is increasing evidence to show that these receptor-ligand interactions play a pivotal role in a number of pathol. situations. Inhibition of receptor activation by VEGF-C and VEGF-D could therefore be pharmaceutically useful. Furthermore, to understand the different roles of VEGF-C, VEGF-D, VEGFR-2 and VEGFR-3 in pathol. situations it will be necessary to dissect the complex interactions of these ligands and their receptors. To facilitate such studies we cloned, sequenced and characterized the expression of rat VEGF-C and VEGF-D. We showed that Cys152→Ser mutants of processed rat VEGF-C can activate VEGFR-3 but not VEGFR-2, while the corresponding mutation in rat VEGF-D inhibits its ability to activate both VEGFR-2 and VEGFR-3. We also synthesized and characterized indolinones that differentially block VEGF-C- and VEGF-D-induced VEGFR-3 kinase activity compared to that of VEGFR-2. These tools should be useful in analyzing the different activities and roles of VEGF-C, VEGF-D and their ligands, and in blocking VEGFR-3-mediated lymphangiogenesis.
ST indolinone prepn inhibitor VEGF C VEGF D receptor activation; rat VEGF C VEGF D cloning characterization
IT Phosphorylation, biological
Signal transduction, biological
(characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)
IT Protein sequences
Rattus norvegicus
cDNA sequences
(cloning, sequencing and characterization of rat VEGF-C and VEGF-D)
IT Adrenal gland
Kidney
Lung
Mammary gland
Ovary
Spleen
Tongue
Tyson's gland
(cloning, sequencing, characterization, and tissue distribution of rat VEGF-C and VEGF-D)
IT Lymphatic system
(lymph vessel, endothelium; characterization of indolinones which preferentially inhibit the lymphangiogenic factors VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)
IT Endothelium
(lymphatic; characterization of indolinones which preferentially inhibit the lymphangiogenic factors VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)
IT Kidney
Lung
(toxicity; cloning, sequencing, characterization, and tissue distribution of rat VEGF-C and VEGF-D)
IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(type VEGFR-2; characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type VEGFR-3; characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

IT 384965-73-5 384965-74-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cloning, sequencing and characterization of rat VEGF-C and VEGF-D)

IT 144638-77-7, VEGFR-3 kinase 150977-45-0, VEGFR-2 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

IT 188417-84-7, VEGF C 193363-12-1, VEGF-D
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

IT 355108-88-2, GenBank AY032728 355108-89-3, GenBank AY032729
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; cloning, sequencing and characterization of rat VEGF-C and VEGF-D)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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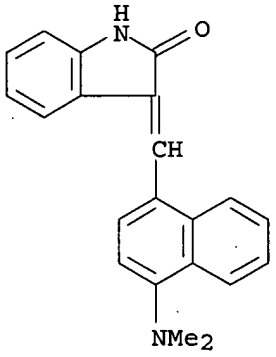
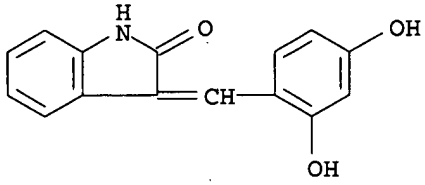
IT **163655-37-6P 328106-29-2P 384832-65-9P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(characterization of indolinones which preferentially inhibit VEGF-C and VEGF-D-induced activation of VEGFR-3 rather than VEGFR-2)

RN 163655-37-6 HCAPLUS
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 328106-29-2 HCAPLUS
CN 2H-Indol-2-one, 3-[(2,4-dihydroxyphenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 384832-65-9 HCAPLUS
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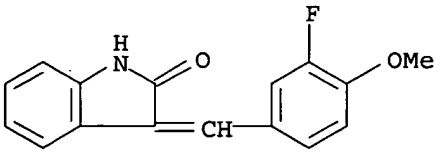


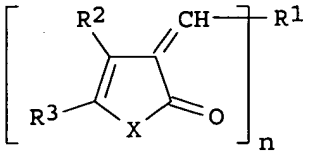
L14 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:599524 HCAPLUS
DN 122:316911
ED Entered STN: 09 Jun 1995
TI Dyes, their preparation, and bulk dyeing of plastics therewith.
IN Roschger, Peter
PA Bayer A.-G., Germany
SO Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C09B023-00
ICS C09B023-04; C09B023-10; C08K005-34; C08K005-15
CC 41-5 (Dyes, Organic Pigments, Fluorescent Brighteners, and Photographic Sensitizers)
Section cross-reference(s): 38, 40
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 632102	A1	19950104	EP 1994-109171	19940615
	EP 632102	B1	19970402		
	R: CH, DE, FR, GB, LI				
	DE 4321420	A1	19950105	DE 1993-4321420	19930628
	DE 4340560	A1	19950601	DE 1993-4340560	19931129
	JP 07018586	A2	19950120	JP 1994-163334	19940623
	US 5626633	A	19970506	US 1995-566317	19951201
PRAI	DE 1993-4321420	A	19930628		
	DE 1993-4340560	A	19931129		
	US 1994-263222	B1	19940621		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 632102	ICM	C09B023-00
	ICS	C09B023-04; C09B023-10; C08K005-34; C08K005-15
EP 632102	ECLA	C08K005/1535; C08K005/3415; C09B023/00D; C09B023/00S; C09B023/04; C09B023/10B
DE 4321420	ECLA	C08K005/1535; C08K005/3415; C09B023/00D; C09B023/00S; C09B023/04; C09B023/10B
DE 4340560	ECLA	C08K005/1535; C08K005/3415; C09B023/00D; C09B023/00S; C09B023/04; C09B023/10B
US 5626633	NCL	008/506.000; 008/512.000; 008/516.000; 008/565.000; 008/568.000; 008/569.000; 008/574.000; 008/576.000; 008/578.000; 008/579.000
	ECLA	C08K005/1535; C08K005/3415; C09B023/00D; C09B023/00S; C09B023/04; C09B023/10B

OS MARPAT 122:316911
GI



I

AB The dyes I (n = 1, 2; R1 = aryl, heterocyclic group for n = 1 and direct bond or arylene for n = 2; R2, R3 = H, organic group: R2R3 = annellated ring; ; X = O, amino) are obtained from R1H or R1CH:Y (Y = O, amino compound) and the appropriate coreactant at 0-250°. Thus, 4-(dimethylamino)benzaldehyde was condensed with benzofuranone to give the dimethylaminobenzylidene derivative which could be used in the coloration of polystyrene.

ST dye plastic coloration

IT Polyamides, processes
Polycarbonates, processes
Polyesters, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(dyes for bulk dyeing of plastics)

IT Dyes
(for bulk dyeing of plastics)

IT Dyeing
(bulk, of plastics)

IT 1090-41-1P 3051-47-6P 3051-50-1P 5812-07-7P 38711-15-8P
50793-69-6P 65155-71-7P 77811-51-9P 163655-03-6P 163655-04-7P
163655-05-8P 163655-06-9P 163655-07-0P 163655-08-1P 163655-09-2P
163655-10-5P 163655-11-6P 163655-12-7P 163655-13-8P 163655-14-9P
163655-15-0P 163655-16-1P 163655-17-2P 163655-18-3P 163655-19-4P
163655-20-7P 163655-21-8P 163655-22-9P 163655-23-0P 163655-24-1P
163655-25-2P 163655-26-3P 163655-27-4P 163655-28-5P 163655-29-6P
163655-30-9P 163655-31-0P 163655-32-1P 163655-33-2P 163655-34-3P
163655-35-4P 163655-36-5P **163655-37-6P** 163655-38-7P
163655-39-8P 163655-40-1P 163655-41-2P 163655-42-3P 163655-43-4P
163655-44-5P 163655-45-6P 163655-46-7P 163655-47-8P
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); PREP (Preparation); PROC (Process); USES (Uses)
(dyes for bulk dyeing of plastics)

IT 9002-89-5 9003-53-6, Polystyrene 9003-54-7, Acrylonitrile-styrene copolymer 9011-14-7, PMMA 25038-54-4, Nylon 6, processes 25038-59-9, Poly(ethylene terephthalate), processes 26284-39-9, Acrylonitrile-methacrylonitrile-styrene copolymer
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(dyes for bulk dyeing of plastics)

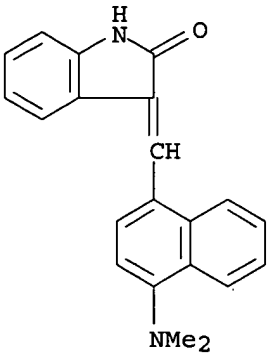
IT 163655-48-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; dyes for bulk dyeing of plastics)

IT 84-83-3 87-41-2, 1(3H)-Isobenzofuranone 100-10-7 123-11-5, 4-Methoxybenzaldehyde, reactions 591-12-8, α-Angelicalactone 2051-95-8, 3-Benzoylpropionic acid 4352-63-0, Naphtho[2,1-b]furan-2(1H)-one 4735-75-5 6050-80-2, Naphtho[1,2-b]furan-2(3H)-one 19828-45-6 31722-17-5 32438-34-9 80162-58-9 96838-79-8 103893-13-6 104094-17-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; dyes for bulk dyeing of plastics)

IT 59-48-3P 61-70-1P, 1-Methyl-2-indolone 92-14-8P, 4-(Diethylamino)-2-methylbenzaldehyde 623-27-8P, Terephthalaldehyde 1971-81-9P, 4-(Dimethylamino)-1-naphthalenecarboxaldehyde 3446-89-7P, 4-(Methylthio)benzaldehyde 14152-56-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(starting material; dyes for bulk dyeing of plastics)

IT **163655-37-6P**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); TEM (Technical or engineered material use); PREP (Preparation); PROC (Process); USES (Uses)
(dyes for bulk dyeing of plastics)

RN 163655-37-6 HCAPLUS
CN 2H-Indol-2-one, 3-[[4-(dimethylamino)-1-naphthalenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)



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E DEVRIES G/AU
L2 7 S E3,E8,E12,E13
E DE VRIES G/AU
L3 132 S E3,E13,E23-E25
E VRIES /AU
E ALLERGAN/PA,CS
L4 985 S ALLERGAN?/PA,CS
SEL RN L1

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L5 10 S E1-E10
L6 3 S L5 AND NC4-C6/ES AND NR>=3
SEL RN
L7 0 S E11-E13/CRN

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L8 0 S L6

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L9              3 S L6

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L11             1 S MAE87 OR MAE 87
L12             5 S L10,L11
L13             1 S L12 AND L1-L4
L14             5 S L12,L13

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